CALCITONIN AND INTESTINAL CALCIUM ABSORPTION

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SUMMARY

The effect of calcitonin (CT) on small intestinal calcium absorption was studied using Thiry-Vella loops in one intact sheep, one intact pig and three parathyroidectomized pigs. Net calcium absorption rate was measured after recirculating through the loop a known volume of a solution containing calcium and polyethylene glycol 4000. Calcitonin was infused intravenously and its effect on the net calcium absorption rate was measured. When relatively high doses of CT (10 mu./min/kg) were infused for up to 45 h, there was an initial rise in net calcium absorption associated with hypocalcaemia, followed by a marked reduction in calcium absorption. When small doses of CT (0.5 mu./min/kg) were infused for 100 h, the increase in the net absorption rate was not observed or was less marked, but there was a significant reduction in net calcium absorption 2 days after the CT infusion was stopped. A reduction in net calcium absorption rate was seen both in intact and parathyroidectomized animals. In one experiment in which the true absorption rate of calcium from lumen to blood was measured using ⁴⁷Ca, a reduction in unidirectional transfer of calcium from lumen to blood was seen 2 days after the CT infusion was stopped. The possible mechanism of this action of CT and its significance in calcium homeostasis during the ingestion of a high calcium diet is discussed.

INTRODUCTION

Calcium metabolism is controlled by three major organs: bone, gut and kidney. Parathyroid hormone (PTH) and 1,25-dihydroxycholecalciferol (1,25 DHCC), two of the hormones influencing calcium metabolism, are said to act on all three of these organs (Parsons & Potts, 1972; Omdahl & DeLuca, 1973). In several species, it is well established that calcitonin (CT) inhibits bone resorption and in some species it also acts on the kidney. However, there is disagreement as to whether CT affects calcium absorption from the gut. In earlier studies, Kenny & Heiskell (1965) and Hirsch, Voelkel & Munson (1964) demonstrated that the acute hypocalcaemic action of CT is independent of the gut. Furthermore, other workers (Krawitt, 1967; Cramer, Parkes & Copp, 1969) did not find any change in calcium absorption after a single large intravenous injection of CT. However, Care (1970) reported that
prolonged administration of CT was capable of inhibiting calcium absorption from the intestine of sheep, a finding which received support from the work of Olson, DeLuca & Potts (1972), using an in-vitro rat intestinal perfusion technique. The present study was undertaken to investigate this apparent discrepancy. Since it was suggested that long-term CT treatment might induce secondary hypersecretion of parathyroid hormone, part of the work reported here was done in parathyroidectomized animals.

**MATERIALS AND METHODS**

One adult Merino sheep and four Large-White pigs (3–6 months of age) were used in the study. Thiry-Vella loops were surgically isolated in all the animals as chronic preparations. A loop of ileum, 160 cm long and 510 cm from the pylorus, was isolated in the sheep and in all the pigs loops of jejunum about 100 cm in length were isolated in this way. Ileum in the sheep and jejunum in the pig were selected because these sites have been shown to be the major sites of absorption of calcium in these species (Moore & Tyler, 1955; Care & van’t Klooster, 1965). Parathyroidectomy was done in one pig before, and in two pigs after, the abdominal operation. The plasma calcium concentration was measured 3 days later, after an overnight fast, and was found to be low in all three pigs, confirming the effectiveness of the operation.

**Measurement of absorption**

The net absorption rate of calcium was measured in the Thiry-Vella loops using a method in which the loop was made part of a semi-closed circuit after catheterization of the two stomata forming the ends of the Thiry-Vella loop with Foley catheters (14 gauge). The loop was first washed out with the fluid to be used and cleared of residual fluid by gentle air pressure. A measured volume of a solution containing polyethylene glycol 4000 (Table 1) was pumped through the loop at a rate of 3 ml/min using a peristaltic pump. Polyethylene glycol 4000 was used as a non-absorbable, stable marker. The composition of the fluids used was based upon that employed by Care & van’t Klooster (1965) for sheep small intestine and upon the analysis of the ultrafiltrate of porcine small intestinal contents. The solution was warmed to body temperature before it entered the loop of intestine. The effluent coming out of the loop was recirculated and the perfusion was continued for 1–2 h. At the end of the perfusion period, the solution remaining in the loop was gently blown through and the final volume estimated from the change in concentration of the non-absorbable marker. A sample of this effluent was acidified by adding 1 ml concentrated hydrochloric acid (A.R. grade) to 50 ml effluent and was kept at 4 °C until it was analysed. The calcium absorption rate was measured over several periods each day, for several days before starting the CT infusion, during the infusion and for 7–10 days after the CT infusion.

To measure the unidirectional absorption rate of calcium from the loop, a known amount of $^{47}$Ca was added to the perfusion solution and absorption of both total calcium and $^{47}$Ca were measured as before.
Calcitonin infusion

Porcine CT (Armour Pharmaceuticals) or salmon CT was dissolved in 0.14 M-sodium chloride solution containing 0.1% (w/v) bovine or porcine serum albumin at pH 4.5. Salmon CT was used in some experiments because it has a longer half-life in blood than porcine CT (Copp, Brooks, Low, Newsome, O’Dor, Parkes, Walker & Watts, 1970). The CT solution was infused intravenously either into the jugular vein in the case of the sheep, or into a leg vein in the case of the pig. Blood samples were obtained before, during and after infusion for the measurement of plasma calcium concentration.

Table 1. Composition of the solutions used for perfusion of Thiry-Vella loops in pigs and sheep

<table>
<thead>
<tr>
<th></th>
<th>Pig</th>
<th>Sheep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride</td>
<td>120 mequiv./l</td>
<td>85 mequiv./l</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>25 mequiv./l</td>
<td>13 mequiv./l</td>
</tr>
<tr>
<td>Magnesium chloride</td>
<td>20 mequiv./l</td>
<td>15 mequiv./l</td>
</tr>
<tr>
<td>Calcium lactate</td>
<td>20 mequiv./l</td>
<td>23 mequiv./l</td>
</tr>
<tr>
<td>Glucose</td>
<td>20 g/l</td>
<td>15 g/l</td>
</tr>
<tr>
<td>Polyethylene glycol 4000</td>
<td>1 g/l</td>
<td>1 g/l</td>
</tr>
</tbody>
</table>

Analyses

Calcium

The calcium concentrations in the perfusion inflow and effluent solutions were measured by the automated method of Gitelman (1967), after suitable dilution. Plasma calcium concentrations were measured by titration against ethylenediaminetetra-acetic acid with murexide as indicator using a photoelectric titrator (Evans Electro Selenium Ltd, Halstead). The plasma calcium concentration was corrected for changes in total solids as described by Care, Duncan & Webster (1967).

$^{47}$Calcium

Radioactivity from $^{47}$Ca was counted in a well-type scintillation counter using a sodium iodide crystal (I.C.N. Tracer Laboratories, Weybridge). A pulse height analyser was used to exclude activity from its decay product, $^{47}$Sc. A 3-ml volume of either standard, perfusion solution or effluent was counted and all counts were corrected for background and radioactive decay.

Polyethylene glycol 4000

This was estimated turbidimetrically according to the method of Hyden (1955). The only modification of the method was in measuring the turbidity at 7.5 min instead of 5 min after the addition of the trichloroacetic acid–barium chloride mixture.

Net calcium absorption rate was calculated according to the formula: net calcium absorption rate in mg/period of perfusion = $V_0[C_0 - (P_0/P_1)C_1]$, where $V_0$ is the volume of the original perfusion solution; $C_0$ and $C_1$ are the calcium concentrations in mg/ml in the original solution and effluent, respectively; $P_0$ and $P_1$ are the poly-
ethylene glycol concentrations in mg/ml in the original solution and effluent, respectively. The absorption rate of calcium from lumen to blood was calculated as a percentage by the formula: percentage unidirectional absorption of calcium per period of perfusion = \[ \frac{R_0 - (P_0/P_1)R_1}{(R_0 + R_1/2)} \times 100, \] where \( R_0 \) and \( R_1 \) are radioactivities due to \( ^{47}\text{Ca} \) in the original solution and effluent, respectively.

RESULTS

Intact animals

Figure 1 shows the effects of infusing 41 mu. porcine CT/min/kg intravenously into a sheep with intact parathyroid glands on 3 successive days for 2, 5 and 3 h, respectively, after an intravenous priming dose of 2-0 i.u./kg each day. Plasma CT levels on the last day of infusion were maintained for a further 3 h by intravenous injections. The rate of administration of CT used here was very high compared with the basal secretion rate of 0-1 mu. CT/kg/min measured in young pigs (Leggate, Care & Frazer, 1969). On the second day of infusion there was an increase in the unidirectional absorption rate of calcium without any significant change in secretion rate and on the following day there was a reduction in both unidirectional and net absorption rate. Both absorption and secretion of calcium returned to pre-infusion levels 3 days later.

In a similar experiment in which salmon CT was infused at the rate of 1-0 mu./min/kg for 7 h on the first day and porcine CT at the rate of 12 mu./min/kg for 5 h on the next 2 days, there was a significant reduction in net absorption rate of calcium. Unidirectional absorption was not measured in this experiment.
The effect of CT infusion on the net calcium absorption rate in a pig with intact parathyroid glands is shown in Table 2. On day 2 there was a significant increase in net absorption when compared with days 0 and 1 \((P < 0.01)\) but the difference was no longer significant if compared with the average absorption rate of calcium before the start of the infusion.

During infusion of CT the plasma calcium concentration decreased from 4.8 to 3.6 mequiv./l. The net calcium absorption rate gradually decreased from day 2 onwards and on day 4 there was a significant reduction in the net absorption rate of calcium.

**Table 2. Effect of calcitonin infusion (CT) on net calcium absorption in an intact pig (means ± S.E.M.)**

<table>
<thead>
<tr>
<th>Days</th>
<th>Rate of i.v. infusion of CT</th>
<th>Net calcium absorption (mg/period of perfusion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>—</td>
<td>16.3 (2)</td>
</tr>
<tr>
<td>-4</td>
<td>—</td>
<td>17.1 ± 0.4 (4)</td>
</tr>
<tr>
<td>0</td>
<td>5.5 mu. salmon CT/min/kg for 4 h</td>
<td>13.7 ± 0.3 (3)</td>
</tr>
<tr>
<td>1</td>
<td>7.6 mu. porcine CT/min/kg for 4 h</td>
<td>13.4 ± 0.5 (4)</td>
</tr>
<tr>
<td>2</td>
<td>5.5 mu. salmon CT/min/kg for 4 h</td>
<td>18.1 ± 2.0 (4)</td>
</tr>
<tr>
<td>3</td>
<td>—</td>
<td>10.3 ± 1.8 (4)</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>3.7 ± 1.1 (4) * (P &lt; 0.001)</td>
</tr>
<tr>
<td>5</td>
<td>—</td>
<td>12.1 ± 4.0 (3)</td>
</tr>
<tr>
<td>6</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

Figures in parentheses are the number of observations.

* Significance of difference from the mean absorption rate on days -4 and -5.

**Parathyroidectomized pigs**

Table 3 shows the results of five experiments in which CT was infused intravenously at varying rates ranging from 0.5–10 mu./min/kg into parathyroidectomized pigs. In the first two experiments the initial increase and the delayed reduction in net calcium absorption seen in earlier experiments with intact animals was also clearly evident. The plasma calcium concentration decreased from 4.98 to 3.54 mequiv./l in experiment 1 and from 4.91 to 2.95 mequiv./l in experiment 2. The rates of infusion of CT, 10 mu./min/kg and 3 mu./min/kg, should be compared with the hypercalcemic secretion rate in similar pigs measured by thyroid perfusion studies (Care, Cooper, Duncan & Orimo, 1968), which can be up to 33 times greater than the basal rate of 0.1 mu./min/kg. As the dose of CT used in these experiments approximates to the upper limit of the physiological range of CT secretion rate, lower infusion rates of CT were used in subsequent experiments.

Infusion of CT at the rate of 1.5 mu./min/kg for 30 h and 0.5 mu./min/kg for 100 h into the pig previously used in experiment 2, had no significant effect on net calcium absorption rate.

In experiments 3, 4 and 5 in which 1.5 and 0.5 mu. CT/min/kg were infused, the initial increase in net calcium absorption rate was not marked (Table 3 and Fig. 2). The plasma calcium concentration decreased by only 0.6 mequiv./l in experiment 3 and by 0.2 mequiv./l in experiment 4. On the other hand, the delayed inhibitory effect of CT on net calcium absorption was clearly seen at these rates of CT infusion. In experiment 5 (Fig. 2) the calcium concentration of the perfusing solution was reduced to 5 mequiv./l. In addition, \(^{47}\)Ca was used to measure unidirectional
Table 3. Effect of different infusion rates of porcine calcitonin (CT) on net calcium absorption rate in parathyroidectomized pigs (means ± S.E.M.)

<table>
<thead>
<tr>
<th>Expt</th>
<th>Rate of i.v. infusion of CT (ml/min/kg)</th>
<th>Before infusion</th>
<th>CT infusion</th>
<th>After infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
<td>Day 3</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>13.0±0.9 (3)</td>
<td>11.8±0.5 (5)</td>
<td>17.9±0.5 (5)</td>
</tr>
<tr>
<td></td>
<td>(for 5 h on 2 days after a priming dose of 100 ml. each day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>19.0±1.5 (3)</td>
<td>25.5±1.9 (5)</td>
<td>26.6±1.3 (7)</td>
</tr>
<tr>
<td></td>
<td>(for 45 h)</td>
<td>NS</td>
<td>**</td>
<td>NS</td>
</tr>
<tr>
<td>3</td>
<td>1.5</td>
<td>18.1</td>
<td>16.8±0.9 (4)</td>
<td>11.2±3.4 (4)</td>
</tr>
<tr>
<td></td>
<td>(for 80 h)</td>
<td>18.1</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>16.4±1.6 (11)</td>
<td>20.4</td>
<td>(2)</td>
</tr>
<tr>
<td></td>
<td>(for 100 h)</td>
<td>16.4±1.6 (11)</td>
<td>20.4</td>
<td>(2)</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>8.3±0.4 (30)</td>
<td>7.3±0.98 (5)</td>
<td>7.4±0.4 (6)</td>
</tr>
</tbody>
</table>

The numbers in parentheses represent the number of observations. Significance of difference from the rates of calcium absorption before CT infusion, except in experiment 3 where it is the difference from the average rate on the first day of infusion. NS, not significant; * P < 0.05; † P < 0.02; ** P < 0.01; *** P < 0.001.

† Day 6.
‡ Day 7.
Calcitonin and intestinal calcium absorption

Fig. 2. Effect of porcine calcitonin on net calcium absorption in a parathyroidectomized pig. Calcitonin was infused at the rate of 0·5 μg/min/kg for 100 h. Black bar indicates period of infusion. The figures in parentheses represent the number of observations. The vertical lines represent ± S.E.M. * P < 0·001 is the significant difference from the mean absorption rate of calcium during days 1–5.

Table 4. Effect of porcine calcitonin (CT) infusion on the unidirectional absorption of calcium in a parathyroidectomized pig (means ± S.E.M.)

<table>
<thead>
<tr>
<th>Day</th>
<th>% Unidirectional absorption/period of perfusion</th>
<th>% Net absorption/period of perfusion</th>
<th>% Secretion/period of perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd day of CT infusion</td>
<td>83·3 ± 4·8 (5)</td>
<td>73·1 ± 3·8 (6)</td>
<td>10·0 ± 0·3 (5)</td>
</tr>
<tr>
<td>2 days after the end of CT infusion</td>
<td>21·4 ± 2·7 (6)</td>
<td>3·3 ± 4·0 (7)</td>
<td>18·1 ± 3·7 (6)</td>
</tr>
</tbody>
</table>

CT was infused at the rate of 0·5 μg/min/kg for 100 h.
The numbers in parentheses represent the number of perfusion periods, each of 1 h duration. NS, not significant.

absorption of calcium. In this experiment, there was no initial increase in the net absorption of calcium. The reduction in net absorption was associated with a reduction in the unidirectional absorption rate of calcium (Table 4). The plasma calcium concentration decreased slightly from 4·8 to 4·6 mequiv./l during infusion of the CT.

DISCUSSION

From these results it is clear that CT, infused for prolonged periods, has an inhibitory effect on intestinal calcium absorption after a delay period of 2–4 days, and also that it has an acute facilitatory effect on absorption which is especially marked.
with high doses. From thyroid perfusion studies with similar pigs, it is known that the basal secretion rate of CT is approximately 0.1 μu/min/kg (Leggate et al. 1969). This secretion rate can increase from 5 to 33-fold during hypercalcaemia, depending on the sensitivity of the porcine thyroid gland. Thus the CT infusion rates were close to or well within the physiological range.

The delayed inhibitory effect of CT shown in this study should be compared with the absence of an acute effect of CT on calcium absorption from the gut found by several groups of workers either indirectly in rats (Hirsch et al. 1964; Kenny & Heiskell, 1965; Aliapoulios, Savery & Munson, 1965) or directly in rats or dogs (Krawitt, 1967; Robinson, Matthews & MacIntyre, 1968; Cramer et al. 1969) and confirmed by ourselves using the direct measurement of the Ca absorption rate in pigs. In all these studies, either a single injection of CT, or short-term treatment with CT was used to examine its early effect on the absorption of calcium.

On the other hand, a long-term injection of CT into rats and into man has produced different results. Wase, Peterson, Rickes & Solewski (1966) found that injection of CT into intact rats for 5 days was followed by an improved calcium balance. Similarly, Woodhouse, Bordier, Fisher, Joplin, Reiner, Kalu, Foster & MacIntyre (1971) injected 0.5 mg synthetic human CT per day intramuscularly into human subjects with Paget’s disease and found that such long-term treatment (up to 9 months) was associated with an increased calcium absorption and an improved calcium balance. Similar findings have been reported by Canniggia, Gennari, Bencini, Cesari & Borrello (1970) and Shai, Baker & Wallach (1971). It has been suggested that this increase is due to increased PTH secretion (Woodhouse et al. 1971), and Jowsey, Riggs, Goldsmith, Kelly & Arnaud (1971) found increased levels of immunoreactive PTH in osteoporotic subjects after prolonged treatment with CT. Thus, the lack of an inhibitory effect of CT on Ca absorption reported by other workers could be explained as follows. (i) In short-term studies in which CT was given for only very brief periods, absorption was not measured for the several days after this CT treatment. (ii) In long-term studies, increased PTH secretion may have counteracted any inhibitory effect on Ca absorption brought about by the CT.

Our finding is in agreement with that of Barlet (1973) who found that faecal excretion of calcium and phosphorus increases after long-term infusion of CT to both parathyroidectomized and intact lambs. Although there is a superficial agreement between our findings and those of Olson et al. (1972), the time course of effect of CT is markedly different. We found a delayed effect, whereas Olson et al. (1972) reported an immediate effect of CT. Although these workers also used physiological doses of CT, the exact physiological status of their isolated vascular perfused rat small intestine was not clear.

There is general agreement that the efficacy of calcium absorption from the gut varies inversely with the dietary calcium intake (Morrissey & Wasserman, 1971) but the mechanism whereby this is brought about is still not understood. Earlier workers (Nicolaysen, Eeg-Larsen & Malm, 1953) implicated bone as the controlling organ, but Boyle, Gray & DeLuca (1971) claimed that 1,25 DHCC is probably the agent controlling the absorption of calcium when dietary intake of calcium is varied. They showed that during dietary calcium deficiency there is increased synthesis of 1,25 DHCC by the kidney. This is probably brought about by an increased secretion
Table 5. Effect of different infusion rates of porcine calcitonin (CT) on net water absorption rate in parathyroidectomized pigs (means ± SEM)

<table>
<thead>
<tr>
<th>Exp</th>
<th>Before infusion of CT</th>
<th>CT infusion</th>
<th>After infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>1</td>
<td>36.7 ± 1.3 (3)</td>
<td>23.4 ± 2.0 (5)</td>
<td>S ** NS</td>
</tr>
<tr>
<td>2</td>
<td>16.0 ± 8.9 (3)</td>
<td>-4.0 ± 7.6 (6)</td>
<td>-14.9 ± 6.2 (7)</td>
</tr>
<tr>
<td>3</td>
<td>-18.6 (2)</td>
<td>-5.3 ± 15.1 (4)</td>
<td>-1.3 ± 7.2 (4)</td>
</tr>
<tr>
<td>4</td>
<td>-30.3 ± 10.4 (11)</td>
<td>-33.6 (2)</td>
<td>S NS</td>
</tr>
<tr>
<td>5</td>
<td>45.3 ± 5.8 (20)</td>
<td>36.5 ± 8.4 (5)</td>
<td>51.7 ± 5.6 (6)</td>
</tr>
</tbody>
</table>

S. The days when calcium absorption rate was significantly different from that before CT infusion (see Table 3). Significance of difference from water absorption before CT infusion: NS, not significant; *P < 0.05; **P < 0.01; ***P < 0.001.
The infusion rates of CT are given in Table 3.
The numbers in parentheses represent the number of observations.
† Day 6.
‡ Day 7.
of PTH (Fraser & Kodicek, 1973). On the other hand, when animals are fed a high calcium diet, the work of Mueller, Anast & Breitenbach (1970) suggests that there is increased CT secretion. Our results clearly show that prolonged administration of CT can reduce calcium absorption from the intestine. Thus, it is likely that CT may play an important role in reducing calcium absorption during dietary calcium excess.

The mechanism for such an effect has been suggested by the findings of Rasmussen, Wong, Bikle & Goodman (1972) who showed that physiologically significant concentrations of CT (5–10 ng/ml) reduced the synthesis of 1,25-DHCC from 25-hydroxycholecalciferol by kidney tubules in vitro. 1,25-Dihydroxycholecalciferol has been shown to act on the intestine to increase the synthesis of calcium binding protein by epithelial cells and thereby increase calcium absorption (Corradino, 1973). On the other hand, the rate of disappearance of Ca binding protein depends on the turnover rate of epithelial cells (Taylor & Wasserman, 1972). Thus, the delayed inhibitory effect of CT on intestinal calcium absorption can be explained in terms of a reduction in the production of 1,25 DHCC by the kidney and a consequent reduction in Ca binding protein in the small intestinal mucosa as new mucosal cells are produced to replace those sloughed away. The rate of regeneration of these cells is about 5 days in human jejunum (Creamer, 1967) but no data are available for a Thiry–Vella loop of porcine or ovine small intestine. The time lag in the development of the inhibitory effect of CT on calcium absorption might thus explain the negative findings obtained in acute experiments.

The inhibitory effect of CT on calcium absorption could also be explained by a non-specific effect of CT on the cellularity of the intestinal mucosa. In order to exclude this possibility, the absorption of water was examined (Table 5). For comparison, the days on which calcium absorption was significantly reduced are also given. In only one experiment was there a significant reduction in water absorption accompanying similar changes in calcium absorption and in two experiments (3 and 4) there was no significant reduction in water absorption. In the remaining two experiments (1 and 2), although there was a significant reduction in water absorption, on one or two of the days when calcium absorption was low, no consistent correlation could be found. Thus, it seems unlikely that the reduction in calcium absorption after CT infusion was mediated through a reduction in the number of mucosal cells.

Since the initial concentration of calcium ions in the perfusion fluid was approximately six times that in plasma, it was considered possible that a marked reduction in calcium concentration in the intestinal loop as a result of net water inflow might have limited the rate of diffusion of calcium from the loop into the blood. However, the difference between the concentration of calcium in the perfusion fluid at the beginning and end of the perfusing period was not great, irrespective of the stage of the experiment, so that it seems unlikely that a significant error was introduced in this way.

The other significant finding in our studies was the increase in net calcium absorption often observed during the infusion of CT. This effect was especially marked when high doses of CT were used and when hypocalcaemia was marked. Hypocalcaemia tends to increase the chemical gradient between the lumen of the gut and blood, which favours increased absorption of calcium, and also reduces secretion of
calcium into the gut from the blood. Both these factors increase net absorption of calcium. Moseley & Axford (1972), using a triple lumen technique in sheep, found that increasing the plasma calcium concentration by infusion of calcium borogluconate decreased the rate of calcium uptake by the small intestine to 18% of the control value. Conversely, infusion of ethylenediaminetetra-acetic acid significantly increased the rate of calcium absorption from the small intestine. These findings support our hypothesis that the increase in calcium absorption seen with the high dose of CT was probably due to hypocalcaemia.

It is concluded that the intravenous infusion of CT for prolonged periods reduces the absorption of calcium from the intestine, perhaps by inhibiting the conversion of 25 hydroxycholecalciferol to 1,25 DHCC, thus leading to a reduction in intestinal calcium binding protein. This may indicate a role for CT in calcium homeostasis during the ingestion of a high calcium diet.

The technical assistance of Mr R. Dowson and Miss S. McWhinnie and the surgical assistance and advice of Dr R. N. B. Kay are gratefully acknowledged. Part of this work was supported by grants from the Medical Research Council and the Agricultural Research Council. Porcine calcitonin was generously donated by Dr J. W. Bastian, Armour Pharmaceutical Co., Kankakee, U.S.A. and the salmon calcitonin was obtained through the kind co-operation of Professor D. H. Copp, University of British Columbia, Canada.

REFERENCES


